

## **SETTLEMENT AGREEMENT**

### **I. PARTIES**

This Settlement Agreement (“Agreement”) is entered into between the United States of America, acting through the United States Department of Justice and on behalf of the Food and Drug Administration ("FDA") and its Center for Biologics Evaluation and Research ("CBER"), the National Institutes of Health ("NIH"), the Office of Acquisition Management and Policy of the Department of Health and Human Services ("HHS"), and the HHS Office of Inspector General (“OIG-HHS”)(collectively the “United States”) and the Trustees of the University of Pennsylvania ("PENN") (hereafter referred to as “the Parties”), through their authorized representatives.

### **II. PREAMBLE**

As a preamble to this Agreement, the Parties agree to the following:

A. The settlement arises out of PENN's participation in the development of an investigational new drug to treat a certain deficiency in an enzyme called ornithine transcarbamylase (OTC). The urea cycle, located in the liver, detoxifies nitrogen and changes it to urea which is nontoxic and can then be excreted as urine. Some individuals are unable to convert nitrogen (ammonia) to urea because they are born with deficient or absent activity of OTC, an essential enzyme for making urea. A high level of ammonia is toxic to the central nervous system, and as a result hyperammonaemic coma and death may occur with OTC deficiency (OTCD).

B. A Phase I safety study of the use of a genetically engineered adenovirus being inserted into human subjects to address OTCD was reviewed by the FDA and NIH. The OTC gene was placed inside a virus called adenovirus, and the virus was injected into the liver through blood vessels. The virus then carried the OTC gene into the research participant's liver cells and once in the liver cells, the OTC gene was to produce the OTC enzyme that is missing in OTCD.

The studies of the safety of this drug in humans were regulated by the FDA. The research studies were funded by the NIH and by the FDA.

C. The Institute for Human Gene Therapy (IHGT) was a center operated by PENN, which was legally responsible for its actions. Two of the three researchers who led the OTCD study, Dr. James Wilson and Dr. Steven Raper were and remain employed by PENN; IHGT is no longer in existence.

D. The Office of Research Services, a component of PENN's central administration, was the entity responsible for grant and contract administration and financial management. PENN had the legal duty to exercise adequate oversight in connection with federal grants awarded to it by the federal government.

E. PENN, as the Applicant Organization for federal funds, certified and accepted the obligation to comply with HHS regulations and Public Health Service policies applicable to human research participants and vertebrate animals.

F. The United States contends that it has certain civil claims against PENN as a result of the actions of its employees in their studies of this new investigational drug described in paragraphs A-E above between July 1998 through September 1999: false statements and claims in connection with the submission of grant applications, progress reports, and annual reports to, and receipt of federal funds from, the NIH; false statements and claims in connection with submissions to the FDA; false statements and claims in connection with the failure to obtain properly informed consent from human research participants; and false statements made to Institutional Review Boards charged with oversight of this research. In addition, the allegations contained in the FDA's Notice of Opportunity for Hearing issued to Dr. Wilson on February 8, 2002, the FDA Form 483 issued to Dr. Wilson on January 19, 2000, the FDA Form 483 issued to

Dr. Wilson on March 1, 2000, the FDA warning letter issued to IHGT on March 3, 2000, the FDA warning letter issued to IHGT on July 3, 2000, the FDA Notice of Initiation of Disqualification Proceedings and Opportunity to Explain (NIDPOE) issued to Dr. Wilson on November 30, 2000, FDA correspondence to Dr. Wilson dated October 27, 2000, November 27, 2000, and March 9, 2001, the FDA warning letter to Dr. Steven Raper dated November 30, 2000, and the FDA letter regarding inspection of manufacturing dated March 13, 2001, which are incorporated herein by reference. The United States' contentions described above are hereinafter referred to as the "Covered Conduct."

G. PENN does not admit the contentions of the United States as set forth in Paragraph F above, and to the contrary, contends that its conduct was at all times lawful and appropriate.

H. In order to avoid the delay, uncertainty, inconvenience and expense of protracted litigation of these claims, the Parties reach a full and final settlement as set forth below.

### **TERMS AND CONDITIONS**

NOW, THEREFORE, in consideration of the mutual promises, covenants, and obligations set forth below, and for good and valuable consideration as stated herein, the Parties agree as follows:

1. PENN agrees to pay to the United States the sum of Five Hundred Seventeen Thousand Four Hundred and Ninety-Six Dollars (\$517,496.00) (the "Settlement Amount"). PENN agrees to make payment of the Settlement Amount by electronic funds transfer pursuant to written instructions to be provided by the Office of the United States Attorney, within thirty (30) days of the final execution of this Agreement.

2. The Parties recognize that institutional oversight of clinical research, through Institutional Review Boards (IRBs), is critical to ensuring the accurate reporting of data to the government as well as providing protection to participants in clinical research. To that end, PENN has taken steps to enhance the IRB system oversight of clinical research as set forth in Exhibit 1, which is attached hereto and incorporated herein. In order to protect human research participants, PENN represents that it has successfully developed a comprehensive program to ensure their safety, including but not limited to: (a) mandatory training for all faculty investigators and clinical research coordinators who participate in clinical research; (b) a historical review of physician-sponsored clinical research by an independent Contract Research Organization (CRO); (c) on-going internal monitoring of its clinical research through the creation of the Office of Human Research (OHR), a PENN School of Medicine-based Center; (d) the establishment of a free-standing Department of Bioethics; (e) the development of procedures to address investigators who fail to adhere to the regulatory standards governing clinical research at PENN; and (f) the implementation of supplemental guidelines focusing on the disclosure and prohibition of financial interests in human research. Some of these actions were commenced prior to the OTCD study's termination. PENN agrees to maintain its systems and enhance them as deemed appropriate through its quality assurance program addressing human research participants.

3. While PENN is aware that Dr. Wilson and Dr. Raper are concurrently entering into respective individual settlement agreements with the United States, PENN is not a party to these agreements. PENN recognizes its obligation, as a sponsor and/or grantee organization, to ensure that researchers who have limitations placed on them by the federal government do not violate the terms of their limitations.

4. For a three-year period, PENN agrees to certify to CBER and the NIH, on an annual basis from the date of execution of this Agreement, that it is in compliance with the terms of this Agreement. The certifications shall be sent to the following addresses:

4.1 To the FDA:

Director  
Office of Compliance and Biologics Quality  
Center for Biologics Evaluation and Research  
United States Food and Drug Administration  
1401 Rockville Pike Suite 200N  
Rockville, MD 20852-1448

4.2 To the NIH:

Director, Division of Grants Compliance and Oversight  
Office of Policy for Extramural Research Administration  
National Institutes of Health, DHHS  
6705 Rockledge Drive, Suite 350  
Bethesda, MD 20892-7974

5. Subject to the exceptions in Paragraph 7 below, in consideration of the obligations of PENN as set forth in this Agreement, conditioned upon PENN's payment in full of the Settlement Amount, the United States (on behalf of itself, its officers, agents, agencies and departments) agrees to release PENN, together with its current and former parent corporations, and the successors and assigns of any of them from any civil or administrative monetary claim the United States has or may have under the False Claims Act, 31 U.S.C. §§ 3729-3733; the Program Fraud Civil Remedies Act, 31 U.S.C. §§ 3801-3812; or the common law theories of payment by mistake, unjust enrichment, breach of contract and fraud, for the Covered Conduct.

6. In consideration of the obligations of PENN set forth in this Agreement, and conditioned upon PENN's payment in full of the Settlement Amount as set forth in paragraph 1, HHS agrees to release and refrain from instituting, directing or maintaining any debarment or

administrative claim under 45 CFR Part 76 or 48 CFR Part 9.4 against PENN for the Covered Conduct. Nothing in this Paragraph precludes HHS from taking action against entities or persons, or for conduct and practices, for which claims have been reserved in Paragraph 7, below.

7. Notwithstanding any term of this Agreement, specifically reserved and excluded from the scope and terms of this Agreement as to any entity or person are any and all of the following:

- (a) Any civil, criminal or administrative claims arising under Title 26, U.S. Code (Internal Revenue Code);
- (b) Any criminal liability;
- (c) Except as explicitly stated in this Agreement, any administrative liability, including mandatory exclusion from Federal health care programs;
- (d) Any liability to the United States (or its agencies) for any conduct other than the Covered Conduct;
- (e) Any claims based upon such obligations as are created by this Agreement, including those created by Exhibit 1 attached hereto;
- (f) Any civil or administrative claims for the Covered Conduct against individuals.

8. In the event that PENN fails to comply in good faith with any of the terms of this Agreement, or should any of PENN's representations or warrants be materially false, the United States may, at its sole discretion, exercise one or more of the following rights:

- (a) seek specific performance of this Agreement and the prevailing party shall be entitled to an award of reasonable attorneys fees and costs in its favor; or
- (b) exercise any other right granted by law.

9. PENN waives and will not assert any defenses it may have to any criminal prosecution or administrative action relating to the Covered Conduct, which defenses may be based in whole or in part on a contention that, under the Double Jeopardy Clause in the Fifth Amendment of the Constitution, or under the Excessive Fines Clause in the Eighth Amendment of the Constitution, this Agreement bars a remedy sought in such criminal prosecution or administrative action. PENN agrees that this settlement is not punitive or a penalty in purpose or effect. Nothing in this paragraph or any other provision of this Agreement constitutes an agreement by the United States concerning the characterization of the Settlement Amount for purposes of the Internal Revenue Laws, Title 26 of the United States Code.

10. PENN fully and finally releases the United States, its agencies, employees, servants, and agents from any claims (including attorneys fees, costs, and expenses of every kind and however denominated) which it has asserted, could have asserted, or may assert in the future against the United States, its agencies, employees, servants, and agents, related to the Covered Conduct and the United States' investigation and prosecution thereof.

11. The Settlement Amount that PENN must pay pursuant to this Agreement by electronic wire transfer pursuant to Paragraph 1 above, will not be decreased as a result of the denial of claims for payment to the extent, if any, that such claims are now being withheld from payment by any federal grant program or payer, related to the Covered Conduct; and agrees not to cost transfer any claims from grants related to the Covered Conduct, and agrees not to appeal any such denials of claims.

12. PENN agrees that all costs (as defined in 45 CFR § 74.27, 45 CFR Part 74 and 45 CFR Part 92), whether direct or indirect incurred by or on behalf of Dr. Wilson, Dr. Raper and PENN or their agents, employees, or former employees in connection with: (a) the matters

covered by this Agreement; (b) the Government's audit(s) and civil and any criminal investigation(s) of the matters covered by this Agreement; (c) PENN's, Dr. Wilson's and Dr. Raper's investigation, defense, and corrective actions undertaken in response to the Government's audit(s) and civil and any criminal investigation(s) in connection with the matters covered by this Agreement (including attorney's fees), (d) the negotiation of this Agreement, and (e) the payment made pursuant to this Agreement, are unallowable costs under the cost principles applicable to government grants, contracts, cooperative agreements, and other agreements to which 45 CFR Part 74 and 45 CFR Part 92 applies (hereafter, "unallowable costs"). These unallowable costs will be separately estimated and accounted for by PENN and PENN will not charge such unallowable costs directly or indirectly to any grants, contracts, cooperative agreements, or other agreements with the United States or seek payment for such unallowable costs through any cost report, cost statement, information statement or payment request submitted by PENN or any of its departments or agencies. The parties agree that nothing in this Agreement shall constitute a waiver of any rights the United States may have under 45 CFR § 74.27, 45 CFR Part 74 and 45 CFR Part 92.

13. This Agreement is intended to be for the benefit of the Parties only, and by this instrument the Parties do not release any claims against any other person or entity.

14. PENN expressly warrants that it has reviewed its financial situation and that it currently is solvent within the meaning of 11 U.S.C. § 547(b)(3), and will remain solvent following its payment to the United States hereunder. Further, the Parties expressly warrant that, in evaluating whether to execute this Agreement, the Parties (i) have intended that the mutual promises, covenants and obligations set forth herein constitute a contemporaneous exchange for new value given to PENN, within the meaning of 11 U.S.C. § 547(c)(1), and (ii) have concluded



that these mutual promises, covenants and obligations do, in fact, constitute such a contemporaneous exchange.

15. Each party to this Agreement will bear its own legal and other costs incurred in connection with this matter, including the preparation and performance of this Agreement.

16. PENN represents that this Agreement is freely and voluntarily entered into without any degree of duress or compulsion whatsoever.

17. This Agreement is governed by the laws of the United States. The Parties agree that the exclusive jurisdiction and venue for any dispute arising between and among the Parties under this Agreement will be the United States District Court for the Eastern District of Pennsylvania.

18. This Agreement constitutes the complete agreement between the Parties. This Agreement may not be amended except by written consent of the Parties.

19. The undersigned individuals signing this Agreement on behalf of represent and warrant that they are authorized to execute this Agreement. The undersigned United States signatories represent that they are signing this Agreement in their official capacities and that they are authorized to execute this Agreement.

20. This Agreement may be executed in counterparts, each of which constitutes an original and all of which constitute one and the same agreement.

21. This Agreement is effective on the date of signature of the last signatory to the Agreement.

22. All Parties consent to the United States' disclosure of this Agreement, and information about this Agreement, to the public.

THE UNITED STATES OF AMERICA

PATRICK L. MEEHAN  
United States Attorney  
Eastern District of Pennsylvania

DATED: \_\_\_\_\_

BY: \_\_\_\_\_  
JAMES G. SHEEHAN  
Associate United States Attorney  
United States Attorney's Office  
Eastern District of Pennsylvania

DATED: \_\_\_\_\_

BY: \_\_\_\_\_  
DAVID R. HOFFMAN  
Assistant United States Attorney  
Eastern District of Pennsylvania

DATED: \_\_\_\_\_

BY: \_\_\_\_\_  
LEWIS MORRIS  
Chief Counsel  
Office of Inspector General  
United States Department of  
Health and Human Services

DATED: \_\_\_\_\_

BY: \_\_\_\_\_  
MARC R. WEISMAN  
Director, Office of Acquisition Management  
and Policy  
United States Department of  
Health and Human Services

FOR TRUSTEES OF THE UNIVERSITY OF  
PENNSYLVANIA

DATED: \_\_\_\_\_

BY: \_\_\_\_\_  
ARTHUR H. RUBENSTEIN, MBBCh  
Executive Vice President for the  
Health System  
Dean, University of Pennsylvania  
School of Medicine

DATED: \_\_\_\_\_

BY: \_\_\_\_\_  
LEE J. DOBKIN  
Deputy General Counsel, University  
of Pennsylvania  
Chief Counsel, University of Pennsylvania  
Health System